

CLAIMS

We claim:

1. A method for screening for a bioactive agent capable of binding to a cell cycle protein tankyrase H, said method comprising combining a cell cycle protein tankyrase H and a candidate bioactive agent, and determining the binding of said candidate agent to said cell cycle protein tankyrase H.

2. A method for screening for agents capable of interfering with the binding of a cell cycle protein tankyrase H and p21 comprising:

- a) combining a cell cycle protein tankyrase H, a candidate bioactive agent and a p21 protein; and
- b) determining the binding of said cell cycle protein and said p21 protein.

3. A method according to claim 2 wherein said cell cycle protein and said p21 protein are combined first.

4. A method for screening for an bioactive agent capable of modulating the activity of an cell cycle protein tankyrase H, said method comprising the steps of:

- a) adding a candidate bioactive agent to a cell comprising a recombinant nucleic acid encoding a cell cycle protein tankyrase H;
- b) determining the effect of the candidate bioactive agent on said cell.

5. A method according to claim 4 wherein a library of candidate bioactive agents are added to a plurality of cells comprising a recombinant nucleic acid encoding a cell cycle protein.

6. A method of diagnosing cancer, said method comprising determining the activity of tankyrase H from a test sample of an individual and comparing said level with a control which indicates there is no cancer, wherein an increase in the activity of tankyrase H in the test sample over the control sample indicates that the individual has cancer.

7. A method for screening for a bioactive agent capable of modulating the activity of a cell cycle protein tankyrase H, said method comprising the steps of:

- a) adding a candidate bioactive agent to a reaction mixture, said mixture comprising
 - i) a source of poly ADP-ribose;
 - ii) a recombinant cell cycle protein tankyrase H;
 - iii) a substrate of cell cycle protein tankyrase H; and
- b) determining the effect of the candidate bioactive agent on the PARP activity of said cell cycle protein tankyrase by determining the poly ADP-ribose content of the substrate.

8. The method of claim 7 wherein the source of poly ADP ribose is biotinylated NAD, and the

determination of poly ADP ribose content involves streptavidin-based-detection of biotin.

9. A method for treating an individual with a cell cycle related disorder, said method comprising administering to said individual an inhibitor of TaHo.

10. A recombinant nucleic acid encoding a cell cycle protein comprising a nucleic acid that hybridizes under high stringency conditions to a sequence complementary to that set forth by SEQ ID NO:1 or SEQ ID NO:2.

11. The recombinant nucleic acid of claim 10 wherein said protein binds to p21.

12. A recombinant nucleic acid encoding a cell cycle protein comprising a nucleic acid having at least 85% sequence identity to a sequence as set forth by SEQ ID NO:1 or SEQ ID NO:2.

13. A recombinant nucleic acid according to claim 10 having the sequence set forth by SEQ ID NO:1 or SEQ ID NO:2.

14. A recombinant nucleic acid encoding a polypeptide sequence as set forth by SEQ ID NO:3 or SEQ ID NO:4.

15. An expression vector comprising the recombinant nucleic acid according to any one of claims 10-14 operably linked to regulatory sequences recognized by a host cell transformed with the nucleic acid.

16. A host cell comprising the recombinant nucleic acid according to any of claims 10-14.

17. A host cell comprising the vector of claim 15.

18. A process for producing a cell cycle protein comprising culturing the host cell of claim 16 or 17 under conditions suitable for expression of a cell cycle protein.

19. A process according to claim 18 further comprising recovering said cell cycle protein.

20. A recombinant cell cycle protein encoded by the nucleic acid of any of claims 10-14.

21. A recombinant polypeptide comprising an amino acid sequence having at least 85% sequence identity with the sequence set forth by SEQ ID NO:3 or SEQ ID NO:4.

22. A recombinant polypeptide according to claim 21 wherein said polypeptide binds to p21.

23. A recombinant polypeptide according to claim 21 having an amino acid sequence as set forth by SEQ ID NO:3 or SEQ ID NO:4.

24. An isolated polypeptide which specifically binds to a cell cycle protein according to claim 21.

25. A polypeptide according to claim 24 that is an antibody.

26. A polypeptide according to claim 25 wherein said antibody is a monoclonal antibody.

27. A method for screening for a candidate bioactive agent capable of modulating PARP activity, comprising the steps of:

(i) providing a TaHo protein;

(ii) providing a candidate bioactive agent; and

(iii) providing a source of poly ADP-ribose;

and determining the amount of poly ADP-ribose associated with said TaHo protein, wherein said TaHo protein is encoded by a nucleic acid sequence having at least 90% identity to the nucleic acid sequence set forth in Figure 1 or 2.

28. A method according to Claim 27, wherein said candidate bioactive agent comprises a small molecule.

29. A method according to Claim 27, wherein said candidate bioactive agent comprises a peptide.

30. A method according to Claim 27, wherein said source of poly ADP-ribose is selected from the group consisting of NAD, biotinylated NAD, or radioactively labeled NAD.

31. A method for screening for a candidate agent capable of inhibiting proliferation, comprising the steps of:

(i) contacting a cell comprising a TaHo protein with a candidate bioactive agent; and

(ii) determining cell cycle progression in said cell.

32. A method according to Claim 31, wherein said cell is a tumor cell.

33. A method according to Claim 31, wherein said candidate bioactive agent comprises a small molecule.

34. A method according to Claim 31, wherein said candidate bioactive agent comprises a peptide.

35. A method for inhibiting growth of a tumor cell, comprising contacting said tumor cell with a bioactive agent capable of inhibiting TaHo activity.

36. A method according to Claim 35, wherein said bioactive agent comprises a small molecule.

37. A method according to Claim 36, wherein said bioactive agent comprises an antisense
oligonucleotide.

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